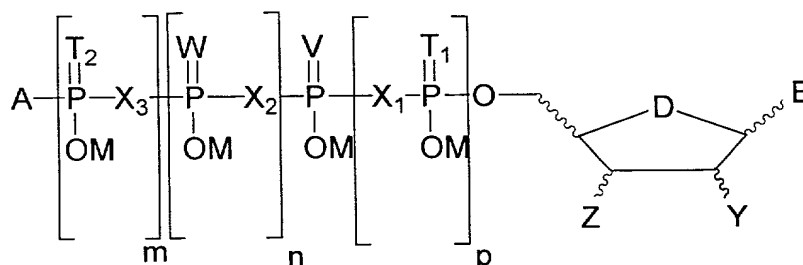


WHAT IS CLAIMED:

1. A compound of Formula I, or a pharmaceutically acceptable salt thereof:

Formula I



10 wherein

A is a covalently bound substituent having a maximum molecular weight of 1000 and is selected from the group consisting of an amino acid, a peptide, a polypeptide, an oligonucleotide, a polynucleotide, a natural or non-natural steroid, OR₁, SR₁, NR₁R₂, and CR₁R₂R₃, wherein R₁, R₂, and R₃ are independently hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, phosphonate, or acylthioalkyl with or without substituents or heteroatoms; or taken together to form a cycloalkyl or aryl ring, with or without substituents or heteroatoms, with the exception of OR₁ and SR₁ not being OH or SH;

X₁, X₂, and X₃ are independently oxygen, methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, or imido;

20 T₁, T₂, W, and V are independently oxygen or sulfur;

m = 0, 1 or 2;

n = 0 or 1;

p = 0, 1, or 2 ;

where the sum of m+n+p is from 0 to 5;

25 M = H or a pharmaceutically-acceptable inorganic or organic counter ion;

D = O or CH₂;

B is a purine or a pyrimidine residue according to general Formulae IV and V which is linked to the 1' position of the furanose or carbocycle via the 9- or 1- position of the base, respectively;

Y = H, OH, or OR₄;

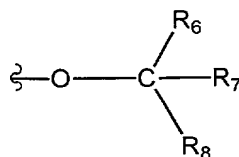
5 Z = H, OH, or OR₅; with the proviso that Y and Z are both not H;

R₄ and R₅ are residues which are linked directly to the 2' and /or 3'

oxygens of the furanose or carbocycle via a carbon atom according to Formula II, or linked directly to the two 2' and 3' oxygens of the furanose or carbocycle via a common carbon atom according to Formula III;

10

Formula II



15

wherein:

O is the corresponding 2' and/or 3' oxygen of the furanose or carbocycle;

C is the carbon atom;

R₆, R₇, and R₈ are H, an alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, or substituted aryl,

20 such that the moiety defined according to Formula II is an ether; or

R₆ and R₇ are H, an alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, or substituted aryl, and

R₈ is alkoxy, cycloalkoxy, aralkyloxy, aryloxy, substituted aralkyloxy, or substituted aryloxy

such that the moiety defined according to formula II is an acyclic acetal or ketal; or

R₆ and R₇ are taken together as oxygen or sulfur doubly bonded to C, and R₈ is alkyl,

25 cycloalkyl, aralkyl, aryl, substituted aralkyl, or substituted aryl, such that the moiety defined according to Formula II is an ester or thioester; or

R₆ and R₇ are taken together as oxygen or sulfur doubly bonded to C, and R₈ is amino or mono- or disubstituted amino, where the substituents are alkyl, cycloalkyl, aralkyl, aryl,

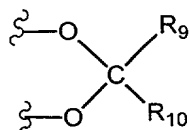
substituted aralkyl, or substituted aryl, such that the moiety according to Formula II is a carbamate or thiocarbamate; or

R₆ and R₇ are taken together as oxygen or sulfur doubly bonded to C, and R₈ is alkoxy, cycloalkoxy, aralkyloxy, aryloxy, substituted aralkyloxy, or substituted aryloxy, such that the

moiety according to Formula II is a carbonate or thiocarbonate; or

R₈ is not present and R₆ and R₇ are taken together as oxygen or sulfur doubly bonded to C and both the 2' and 3' oxygens of the furanose are directly bound to C to form a cyclical carbonate or thiocarbonate;

Formula III

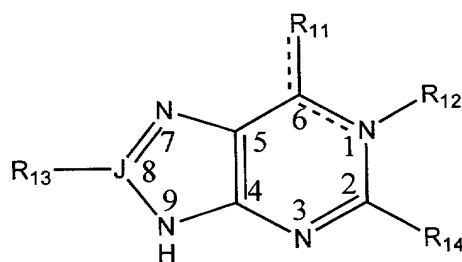


wherein:

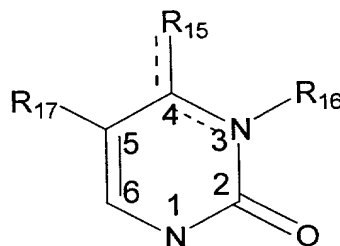
O is the 2' and 3' oxygens of the furanose or carbocycle; and the 2' and 3' oxygens of the furanose or carbocycle are linked by a common carbon atom (C) to form a cyclical acetal, cyclical ketal, or cyclical orthoester;

for cyclical acetals and ketals, R₉ and R₁₀ are independently hydrogen, alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, substituted aryl, or can be joined together to form a homocyclic or heterocyclic ring composed of 3 to 8 atoms, preferably 3 to 6 atoms; for cyclical orthoesters, R₉ is hydrogen, alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, or substituted aryl, R₁₀ is alkyloxy, cycloalkyloxy, aralkyloxy, aryloxy, substituted aralkyloxy, or substituted aryloxy;

Formula IV



Formula V



wherein:

R₁₁ and R₁₅ are hydroxy, oxo, amino, mercapto, alkylthio, alkyloxy, aryloxy, alkylamino, cycloalkylamino, aralkylamino, arylamino, diaralkylamino, diarylamino, or dialkylamino, where the alkyl groups are optionally linked to form a heterocycle; or

R₁₁ and R₁₅ are acylamino, provided that they incorporate an amino residue from the C-6 position of the purine or the C-4 position of the pyrimidine; or

when R₁₁ in a purine or R₁₅ in a pyrimidine has as its first atom nitrogen, R₁₁ and R₁₂ or R₁₅ and R₁₆ are taken together to form a 5-membered fused imidazole ring (etheno compounds), optionally substituted on the etheno ring with alkyl, cycloalkyl, aralkyl, or aryl moieties, as

described for R₆-R₁₀ above;

when R₁₅ in a pyrimidine has as its first atom oxygen, R₁₅ and R₁₇ are taken together to form a 5-membered dihydrofuran ring, optionally substituted on the dihydrofuran ring with alkyl, cycloalkyl, aralkyl, or aryl moieties, as described for R₆-R₁₀ above;

J is carbon or nitrogen, with the provision that when nitrogen, R₁₃ is not present;

5 R₁₂ is hydrogen, O or is absent;

R₁₆ is hydrogen, or acyl (e.g. acetyl, benzoyl, phenylacetyl, with or without substituents);

R₁₃ is hydrogen, alkyl, bromo, azido, alkylamino, arylamino or aralkylamino, alkoxy, aryloxy or aralkyloxy, alkylthio, arylthio or aralkylthio, or ω-E(C₁₋₆ alkyl)G-, wherein E and G are independently amino, mercapto, hydroxy or carboxyl;

10 R₁₄ is hydrogen, chlorine, amino, monosubstituted amino, disubstituted amino, alkylthio, arylthio, or aralkylthio, where the substituent on sulfur contains up to a maximum of 20 carbon atoms, with or without unsaturation;

R₁₇ is hydrogen, methyl, alkyl, halo, alkyl, alkenyl, substituted alkenyl, alkynyl, or substituted alkynyl.

15

2. The composition according to Claim 1, wherein:

A is selected from the group consisting of OR₁, SR₁, NR₁R₂, and CR₁R₂R₃, wherein R₁, R₂, and R₃ are independently hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, phosphonate, or acylthioalkyl with or without substituents or heteroatoms; or taken together to form a

20 cycloalkyl or aryl ring, with or without substituents or heteroatoms, with the exception of OR₁ and SR₁ not being OH or SH;

X₁, X₂, and X₃ are each oxygen;

T₁, T₂, W, and V are each oxygen;

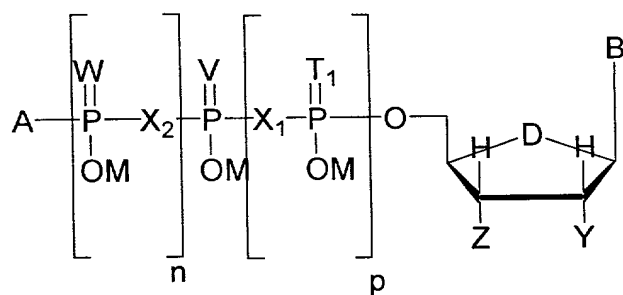
D=O;

25

3 The composition according to Claim 1, wherein Formula I is a compound of Formula Ia:

Formula Ia

30



wherein the variable groups have the definitions as above.

4. The composition according to Claim 3, wherein: A is selected from the group consisting of OR_1 , SR_1 , NR_1R_2 , and $CR_1R_2R_3$, wherein R_1 , R_2 , and R_3 are independently hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, phosphonate, or acylthioalkyl with the exception of OR_1 and SR_1 not being OH or SH; or wherein NR_1R_2 , and $CR_1R_2R_3$ are taken together to form a ring with or without substituents or heteroatoms;
- X₁, X₂, and X₃ are oxygen, dichloromethylene, or difluoromethylene;;
- T₁, T₂, W, and V are oxygen;
- the sum of m+n+p is from 0 to 4;
- M is sodium;
- D is oxygen;
- Y and Z are both OH.
5. A pharmaceutical composition comprising a compound of Formula I of Claim 1 in a pharmacologically acceptable carrier.
6. A compound of Formula I selected from the group consisting of: 2'3'-O-methylenebenzyl β -(cyclohexyl) UDP (5), 2'-phenylcarbamoyl β -benzyl UDP (14), 2'-(phenoxy)formyl β -propyl UDP (15), 6-phenyl-furanopyrimidine riboside β -(3-carboxyphenyl)methyl diphosphate (20), 4-thiobenzyl pyrimidine riboside β -benzyl diphosphate (21), 2',3'-dibenzoyl β -propyl UDP (29), 5-(3-methoxyphenyl)ethenocytosine 2'-deoxy-3'-phenylcarbamoyl riboside β -propyl diphosphate (33), N⁴-propyl-2',3'-dibenzoyl β -benzyl CDP (36), 2'3'-O-methylenebenzyl β -(2-methylpropylphosphono) UDP (37), 2'-phenylcarbamoyl β -(2-carboxyethylphosphono) UDP (48), N⁴-(4-fluorophenylcarbamoyl) β -

- (o-methylbenzylphosphono) CDP (54), 2',3'-di(phenoxy)formyl β -(pentylphosphono) UDP (61), N⁴-propyl-2',3'-dibenzoyl β -(2-carboxyethylphosphono) CDP (72), 2'-deoxy γ -benzyl UTP (77), γ -(thiocyclohexyl) UTP (79), 6-(3-methylphenyl)-furanopyrimidine riboside δ -(2-naphthalenemethyl) tetraphosphate (86), 2'3'-O-methylenebenzyl γ -propyl UTP (93), 5-(3-methylphenyl)ethenocytosine 2'3'-O-methylenebenzyl riboside δ -propyl tetraphosphate (105), 5-(3-methoxyphenyl)ethenocytidine riboside γ -(2-naphthalenemethyl) triphosphate (111), N⁴-(benzyloxyformyl)-2'-deoxy γ -benzyl CTP (115), N⁴,3'-dibenzoyl-2'-deoxy γ -(2-naphthalmethyl) CTP (123), 5-(3-trifluoromethylphenyl)ethenocytidine γ -(1-naphthalenemethylphosphono) triphosphate (135), 4-thiopropyl pyrimidine riboside γ -(4-aminocarboxybutylphosphono) triphosphate (138), 2'3'-O-methylenepheneethyl γ -(3,4-dimethylphenylphosphono) UTP (147), 5-iodo-2'3'-O-methylenebutyl γ -(1-naphthalenemethylphosphono) UTP (157), 2',3'-dibenzoyl δ -(4-ethoxyphenylphosphono) uridine tetraphosphate (161), 2'3'-O-methylenebenzyl γ -(2-naphthalene) ATP (175), 2-thiopropyl-2'3'-O-methylenebenzyl γ -benzyl ATP (180), 2-thiomethyl-N⁶-propyl-2'3'-O-methylenebenzyl γ -(2-naphthalene) ATP (183), 2'3'-O-methylenebenzyl γ -anilino ATP (192), 2'3'-O-methylenebenzyl γ -(carboxymethylphosphono) ATP (200), 2'3'-O-methylenebenzyl δ -(1-naphthalene) adenosine tetraphosphate (201), 2-thiopropyl-2'-deoxy-3'-(3-trifluoromethylphenyl)carbamoyl γ -(4-methoxyphenylphosphono) ATP (212).
7. The composition a according to Claim 6, wherein the compound is selected from the group consisting of: 2'3'-O-methylenebenzyl β -(cyclohexyl) UDP (5), 5-(3-methoxyphenyl)ethenocytosine 2'-deoxy-3'-phenylcarbamoyl riboside β -propyl diphosphate (33), 2'3'-O-methylenebenzyl β -(2-methylpropylphosphono) UDP (37), 2',3'-di(phenoxy)formyl β -(pentylphosphono) UDP (61), 2'3'-O-methylenebenzyl γ -(propyl) UTP (93), 5-(3-methylphenyl)ethenocytosine 2'3'-O-methylenebenzyl riboside δ -propyl tetraphosphate (105), 5-(3-trifluoromethylphenyl)ethenocytidine γ -(1-naphthalenemethylphosphono) triphosphate (135), 2',3'-dibenzoyl δ -(4-ethoxyphenylphosphono) uridine tetraphosphate (161), 2-thiopropyl-2'3'-O-methylenebenzyl γ -benzyl ATP (180), and), 2'3'-O-methylenebenzyl δ -(1-naphthalene) adenosine tetraphosphate (201).

8. A pharmaceutical composition comprising a compound of Formula I of Claim 1 in a pharmaceutically acceptable carrier.

9. The pharmaceutical composition according to Claim 8, wherein the compound is in a formulation selected from the group consisting of: aqueous solution, liquid/liquid suspension, gel, gel-like, and solid formulations.

10. A method of preventing, diagnosing, or treating epithelial or retinal tissue disease or condition of a subject in need of such prevention or treatment; comprising administering to said subject the compound of Formula I of Claim 1 in an amount effective to prevent or treat said epithelial or retinal tissue disease or condition, wherein said epithelial or retinal tissue disease or condition is selected from the group consisting of eye diseases, respiratory diseases, gastrointestinal tract diseases, inflammatory diseases, and allergic diseases.

11. The method according to Claim 10, wherein the process of preventing or treating epithelial or retinal tissue disease or condition associated therewith comprises:

(a) identifying a mammal at risk for epithelial or retinal tissue diseases or condition; and

(b) applying a composition comprising a compound of Formula I in an amount effective to prevent or treat said epithelial or retinal tissue disease or condition associated therewith.

12. The method according to Claim 10, wherein the process of preventing or treating epithelial or retinal tissue disease or condition associated therewith comprises:

(a) applying to a mammal at risk for or presenting epithelial or retinal tissue diseases or condition a composition comprising a compound of Formula I in an amount effective to prevent the incidence of epithelial or retinal tissue diseases or condition, and

(b) determining whether such disease or condition developed or was reduced.

13. The method according to Claim 10, wherein said epithelial or retinal tissue disease or condition is selected from the group consisting of vaginal and cervical dryness, chronic bronchitis, chronic obstructive pulmonary disorder, pneumonia, cystic fibrosis, ciliary

dyskinesia, sinusitis, lung cancer, otitis media, retinal detachment, retinal edema, dry eye, dry mouth, gastroesophageal reflux disease(GERD), diarrhea, irritable bowel disease, constipation, glaucoma associated with elevated intraocular pressure, retinal degenerative diseases, corneal edema, allergic conjunctivitis, ocular surface inflammation, and allergic rhinitis.

14. The method according to Claim 10, wherein said epithelial or retinal tissue disease or condition is a retinal degenerative disease selected from the group consisting of inherited retinal degenerative diseases, acquired retinal degenerative diseases, and inflammation-induced retinal degenerative diseases.

15. The method according to Claim 14, wherein 1) said inherited retinal degenerative disease is selected from the group consisting of macular degeneration, Stargardt's disease, Best's disease, glaucoma, retinitis pigmentosa, and optic nerve degeneration; 2) said acquired retinal degenerative disease is selected from the group consisting of cystoid macular edema, retinal detachment, photic damage, ischemic retinopathies, retinopathies, and peripheral vitreoretinopathy; and 3) said inflammation-induced retinal degenerative disease is selected from the group consisting of viral-, bacterial- or toxin-induced retinal degeneration, optic neuritis, and uveitis.

16. The method according to Claim 10, wherein said epithelial or retinal tissue disease or condition is a respiratory disease and said compound is administered to the lungs of said subject in an amount sufficient to achieve at least one result selected from the group of results consisting of hydrating lung mucus secretions; enhancing ciliary beat frequency; facilitating expectoration; enhancing lung secretion removal; enhancing sputum induction; facilitating lung sample expectoration; and enhancing cough clearance.

17. The method according to Claim 13, wherein said epithelial or retinal tissue disease or condition is an eye disease selected from the group consisting of; a) dry eye disease and said compound is administered to at least one eye of said subject in an amount sufficient to increase hydration and lubrication of ocular surfaces and b) edematous retinal disorders, including retinal detachment and retinal edema, and said compound is administered to at least one eye of said subject in an amount sufficient to stimulate the removal of pathological fluid

accumulation in intra-retinal and subretinal spaces associated with edematous retinal disorders.

18. The method according to Claim 17, wherein the compound used for dry eye disease of a) is administered to the eye in a topical administration carrier vehicle selected from a group consisting of: drops of liquid, liquid wash, gels, ointments, sprays and liposomes and the compound used for edematous retinal disorders of b) is administered to the eye in the form of an liquid in an injection into the vitreous, bolus or sustained infusion into the vitreous, by sustained release into the vitreal cavity, by retrobulbar conjunctival injection, release, or infusion, by transcleral injection, by sustained transcleral release or infusion, by ocular surface instillation, or by acute and chronic injection or infusions.

19. The method according to Claim 10, wherein said administering is by systemic administration involving the administration to said subject said compound of Formula I by a method selected from the group of methods consisting of: a) administering a liquid/liquid suspension of said compound via nose drops or nasal spray; b) administering a nebulized liquid of said compound to oral or nasopharyngeal airways of said subject; c) administering an oral form of said compound including chewable gum; d) administering an injectable form of said compound; e) administering a suppository form of said compound; f) administering an intra-operative instillation of a gel, cream, powder, foam, crystals, liposomes, spray or liquid suspension form of said compound; and g) administering said compound in a form of a transdermal patch or a transdermal pad: such that a therapeutically effective amount of said compound contacts the intended tissues of said subject via systemic absorption and circulation.

20. A method of preventing or treating diseases associated with platelet aggregation and thrombosis in humans and other mammals, comprising administering to a subject a pharmaceutical composition containing the compound of Formula I of Claim 1 in an amount effective to inhibit ADP-induced platelet aggregation.